

# D7.5

## Ethics Expert Panel

### Brief Activity Report

**777450 - PARADIGM**

**Patients Active in Research and Dialogues  
for an Improved Generation of Medicines**

**WP7 – Project Coordination and Management**

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<sup>1</sup> Please choose the appropriate reference and delete the rest:

PU = Public, fully open, e.g. web;

CO = Confidential, restricted under conditions set out in Model Grant Agreement;

CI = Classified, information as referred to in Commission Decision 2001/844/EC.

## Document History

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## Definitions

Partners of the PARADIGM Consortium are referred to herein according to the following codes:

- **EPF.** EUROPEAN PATIENTS FORUM (Luxembourg) – **Project Coordinator**
  - **EURORDIS.** EUROPEAN ORGANISATION FOR RARE DISEASES ASSOCIATION (France)
  - **EATG.** EUROPEAN AIDS TREATMENT GROUP (Germany)
  - **AE.** ALZHEIMER EUROPE (Luxembourg)
  - **AIFA.** AGENZIA ITALIANA DEL FARMACO (Italy)
  - **HTAi.** HEALTH TECHNOLOGY ASSESSMENT INTERNATIONAL (Canada)
  - **IACS.** INSTITUTO ARAGONES DE CIENCIAS DE LA SALUD (Spain)
  - **FSJD.** FUNDACIO SANT JOAN DE DEU (Spain)
  - **VU-ATHENA.** STICHTING VU (The Netherlands)
  - **UOXF-CASMI.** THE CHANCELLOR, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD (United Kingdom)
  - **EFGCP.** EUROPEAN FORUM FOR GOOD CLINICAL PRACTICE (Belgium)
  - **SYNERGIST.** THE SYNERGIST (Belgium)
  - **SYNAPSE.** SYNAPSE RESEARCH MANAGEMENT PARTNERS SL (Spain)
  - **EFPIA.** EUROPEAN FEDERATION OF PHARMACEUTICAL INDUSTRIES AND ASSOCIATIONS (Belgium)
  - **Project Leader**
  - **MSD Corp.** MERCK SHARP & DOHME CORP (United States)
  - **UCB.** UCB BIOPHARMA SPRL (Belgium)
  - **ABPI.** THE ASSOCIATION OF THE BRITISH PHARMACEUTICAL INDUSTRY (United Kingdom)
  - **AMGEN.** AMGEN LIMITED (United Kingdom)
  - **BAYER.** BAYER AKTIENGESELLSCHAFT (Germany)
  - **GSK.** GLAXOSMITHKLINE RESEARCH AND DEVELOPMENT (United Kingdom)
  - **GRT.** GRUENENTHAL GMBH (Germany)
  - **JANSSEN.** JANSSEN PHARMACEUTICA NV (Belgium)
  - **LILLY.** Eli Lilly and Company Limited (United Kingdom)
  - **LUNDBECK.** H. LUNDBECK AS (Denmark)
  - **MERCK.** MERCK KOMMANDITGESELLSCHAFT AUF AKTIEN (Germany)
  - **NOVO NORDISK.** NOVO NORDISK A/S (Denmark)
  - **PFIZER.** PFIZER LIMITED (United Kingdom)
  - **ROCHE.** F. HOFFMANN-LA ROCHE AG (Switzerland)
  - **SERVIER.** INSTITUT DE RECHERCHES INTERNATIONALES SERVIER (France)
  - **VFA.** VERBAND FORSCHENDER ARZNEIMITTELERSTELLER EV (Germany)
  - **SARD.** SANOFI-AVENTIS RECHERCHE & DEVELOPPEMENT (France)
  - **NOVARTIS.** NOVARTIS PHARMA AG (Switzerland)
  - **COVANCE.** COVANCE LABORATORIES LTD (United Kingdom)
  - **ALEXION.** ALEXION SERVICES EUROPE (Belgium)
- **Consortium.** The PARADIGM Consortium, comprising the above-mentioned legal entities
  - **Consortium Agreement.** Agreement concluded amongst PARADIGM participants for the implementation of the Grant Agreement. Such an agreement shall not affect the parties' obligations to the Community and/or to one another arising from the Grant Agreement.

## 1. Publishable Summary

PARADIGM is a short-term project intended to establish a framework that will enable meaningful, impactful, ethical and sustainable patient engagement with multiple stakeholders in the medicines development process. The development of the resulting tools for facilitating this collaboration not only requires intense and ongoing ethical reflections and input but also the collaboration between the Consortium members engaged in finding mutually acceptable solutions for such an engagement framework. The “Applied ethics” approach suggested in the PARADIGM proposal as an innovative concept for maximising ethical input into the concept development and outcome production processes has been developed and is being implemented. The multi-stakeholder Ethics Expert Panel (EEP) has been established. The EEP members have fulfilled the assigned tasks in a flexible, adaptive and constructive manner. Capacity and collaboration have been established to further support the relevant Work Packages and Tasks over the second half of the project. Additional EEP experiences will be made and reflected upon to validate the suitability of such a concept for public-private partnership projects.

## 2. Methods

PARADIGM is an IMI project that intends to create and implement a framework for efficient and ethical patient engagement (PE) with policymakers, the pharmaceutical industry, clinical investigators, regulators, HTA bodies, ethics committees, and the wider health community by delivering a set of recommendations and tools aimed at facilitating patient engagement in medicines development. The PARADIGM Consortium consists of a wide range of stakeholders with different interests, priorities and needs, including vulnerable patient groups, therefore, the opportunities and needs for patient engagement cover a large spectrum of conditions. Consortium constellation and expected outcomes require awareness of the potential for ethical conflicts as well as the availability of ethical competence in how to ensure adherence to ethical principles such as fairness, equity, solidarity, dignity, autonomy, transparency, objectivity and protection of patients’ rights, confidentiality with safeguards in the different areas of collaboration.

In order to allow for pragmatic, critical and transparent ethical input and overview in the work of PARADIGM, the Ethics Expert Panel (EEP) was formed as Task 7.4 in Work Package 7, Project Coordination and Management, enabling the strategy of providing “applied ethical expertise”. To maintain its independence of the Work Packages (WP) involved in the generation of project deliverables, the EEP is not part of the governance structure but has a direct reporting and appeal line to the project co-leaders. EEP members are to provide ethical expertise to the Work Packages’ activities to support the latter’s content discussions throughout, until finalisation of deliverables. In case of difficult ethical questions that cannot be clarified, the respective EEP members are to bring the topic to the full EEP for discussion and resolution. In addition, the EEP is expected to develop general ethical project documents such as the Ethics Framework for the PARADIGM project and the PARADIGM Code of Conduct in collaboration with Work Package 4.2.

Fair and comprehensive representation of the PARADIGM Consortium members and expertise in applied ethics in different aspects of medicines development are essential for the effective and successful work of the EEP. The EEP consists of external experts with ethical and legal backgrounds as well as experts from within the Consortium partner organisations with ethical competence not directly participating in the operational tasks of PARADIGM per se. In addition, the EEP members must provide their ethical expertise to the WPs whenever WPs so require.

This Mid-Term EEP Report presents the EEP’s activities and achievements in the first 12 months of the PARADIGM project.

### 3. Results

The Ethics Expert Panel is chaired by EFGCP, an independent not-for-profit organisation with considerable expertise on ethics issues.

As a first step, the appointed Chair of the Ethics Expert Panel prepared the call for EEP member nominations by defining their required expertise, describing their expected role and time requirements and then set the rules for selection and nomination of the EEP members. The Project Coordinators commented on and approved this nomination process. The call was disseminated to all consortium members and to external ethics experts across Europe.

Finding interested candidates turned out to be challenging. Consortium partners struggled to find suitable candidates and the search for external experts revealed that most persons approached had over-full agendas and problems from an employment point of view to actively work on an IMI project in which their organisation was not a Consortium member. During the course of the project it also transpired that people were changing jobs and responsibilities so that a certain amount of fluctuation could not be avoided. Notwithstanding these difficulties, nominations were received and the EEP was set up.

Currently the EEP consists of representatives from the following organisations:

European Forum for Good Clinical Practice (EFGCP), Katholieke Universiteit Leuven, The Synergist, Roche/Genentech, Instituto Aragonés de Ciencias de la Salud (IACS), Ethics Committee of the University of Groningen, World Federation of Incontinent Patients, Horizon 2020 expert. A call to replace the European Aids Treatment Group (EATG) and EURORDIS representatives who have moved on in their careers, is ongoing. Further efforts are being made to find one or two more representatives from the private Consortium partners.

In a first joint initiative, the EEP developed the PARADIGM Ethics Framework for the Consortium (D7.1) which was carefully reviewed, amended and approved by the Steering Committee before its implementation in Month 4.

This document was created according to the premises listed below:

- A patient's experience and perspective of their disease as well as their views on patient engagement in the medicinal product lifecycle is unique and should therefore be valued as specialist knowledge that is different from the professional knowledge of clinicians, clinical researchers in the pharmaceutical industry and academia, members of ethics committees, regulatory agencies and HTA bodies.
- The perspective of patients is frequently represented by patient organisations which integrate the experience of their members and disseminate this combined knowledge to help improve the disease conditions and quality of life of their members. Carers or parents get involved with patient organisations for those patients unable to decide for themselves due to their physical and/or mental condition or for reasons of age (minors).
- Finding better ways to engage patient organisations and patients into the medicines development and access to treatment process will lead to clinical research and treatments that are better adapted to the real needs of patients. This can generate benefits for all parties in their attempts to accelerate the development of and access to new treatment options.
- The integrity, credibility and independence of all involved partners, as well as the constraints and obligations under which all stakeholders operate, should be respected at all times by all partners.

- Adherence to this PARADIGM Ethics Framework by all PARADIGM Consortium Members and their collaborators ensures a trustworthy and successful execution and completion of the project.

This Ethics Framework was disseminated by the 'Project Coordination' team to all persons listed on the PARADIGM contact list.

An important aspect of the collaboration in PARADIGM is the recognition, proactive identification and addressing of any Conflicts of Interest of the active contributors to the project, thereby ensuring appropriate disclosure when necessary. To enable a thorough, objective review of the potential for Conflicts of Interest, the EEP and Steering Committee decided to develop and disseminate a Declaration of Interest (DoI) form, to be returned to the EEP for review and potentially early detection of a potential Conflict of Interest. EFGCP disseminated the form to all people listed on the PARADIGM contact list with explanations on how to complete and return the signed form.

52 people received the Declaration of Interest Form. As mentioned on page 9 of the D7.1 Ethics Framework, the DoI forms were sent to *'all members of the PARADIGM Steering Committee, Project Team, Ethics Expert Panel, the Task Leaders and the main contacts for all members of the Consortium with the request to complete a personal interest disclosure form describing his/her professional and non-professional activities and affiliations'*. 45 people returned their signed DoI which represents a total percentage of 86.5%. The next joint task of the EEP will be the preparation of the PARADIGM Code of Conduct in collaboration with T4.2. Preparatory work has started.

Ongoing ethical reflections of the work performed in the different Work Packages of PARADIGM are key to the success of the project. However, not all Tasks in PARADIGM contain topics of ethical relevance. The EEP members have analysed the topics of the different WP Tasks and decided which of these would require EEP contributions, at least in part. Based on personal experience, interest and availability, EEP members assigned themselves to the different Work Packages and Tasks.

The following Tasks were selected:

- WP1: Task 1.2: Co-Prioritise minimal expectations for patient engagement across key stakeholders
- WP1: Task 1.3: Develop a set of criteria to assess patient engagement practices and processes against minimal expectations
- WP2: Task 2.1: Select existing and representative practices and processes
- WP2: Task 2.2: Assess identified patient engagement practices and processes
- WP2: Task 2.3: Inventory of patient engagement gaps across the 3 decision-making points (final review only)
- WP3: Task 3.3: Defining frameworks for Measurement & Evaluation of outcomes and impact
- WP3: Task 3.4: Assessment of the M&E frameworks for assessing the outcomes and impact of patient engagement in the medicines development cycle
- WP4: Task 4.1: Development of recommendations on the required capabilities for patient engagement
- WP4: Task 4.2: Development of tools and templates and enhancement and extension of guidances for patient engagement (all EEP members involved in developing the Code of Conduct, several EEP members involved in support to tools development)
- WP5: Task 5.3: Open Patient Engagement Forums
- WP5: Task 5.4: Ongoing storytelling, dissemination & other communication activities
- WP6: Task 6.3: Cross-evaluation of the ecosystem and needs, and definition of potential models to address sustainability of outcomes and concepts of PARADIGM
- WP6: Task 6.4: Definition of the services
- WP6: Task 6.5: Sustainability roadmap (engagement of the complete EEP)

The type and depth of involvement varies in the different Tasks, ranging from participation in regular tele-conferences and phone calls, participation in WP/Task meetings, and contributions to or the review of Task outcomes. Since the PARADIGM Work Plan is built on consecutive Tasks, not all Tasks were active as yet and, on the other hand, a number of Task elements had already been decided in the project proposal stage and were no longer subject to specific ethical advice.

Capacity and processes for relevant ongoing ethical input to support the WPs' and Tasks' outcome production process in the second half of the project have been established and are functioning well.

## 4. Discussion

The PARADIGM “applied ethics” infrastructure and process represent an innovative approach to enable broad, continuous ethical input and support in all Work Packages. This contrasts with the “standard” approach of an Ethics Review Board or even Ethics Approval Board where documents are submitted for an ethical review in a pre-final stage and where the Review Board Members perform an ethical oversight role. Often, such an approach no longer has a major impact on the outcome but prolongs the release process and makes ethical input a threat to timelines for the Task members. The PARADIGM approach enables very early input – as early as during the Tasks’ brainstorming phase and allows for ethical awareness and considerations of all Task members during the Task execution process. The EEP members are integrated and constructive consultants for the Task teams. Delays in finalisation of deliverables can be avoided, especially as the presentation of potentially difficult questions to the full EEP can occur during the outcome development process. On the other hand, documents that require comprehensive ethical expertise like ethical frameworks or codes of conduct can be elaborated by the full ethical expertise alongside the Work Package implementation activities.

This concept had to be developed in detail and implemented in the first 12 months of the project. The WP and Task Leaders were informed about the EEP member(s) assigned to their Task(s) and encouraged to invite the respective EEP member(s) to their routine tele-conferences and work activities. Due to time constraints of EEP members, fluctuation and also due to the type of activity - requiring ethical input or not – and the proactivity of Task leaders, the intensity of this EEP involvement varied considerably. However, the collaboration has worked since no conflicting topic was brought before the EEP by any of the EEP members in the Tasks. The experiences so far will be reflected in an upcoming EEP meeting and potential weaknesses addressed in collaboration with the WP and Task leaders.

PARADIGM is a short duration project and the first 12 months have been dedicated to research, fact-finding and concept development. First experiences with the challenges of implementing such a concept and the type of support that is required from EEP members have been drawn. Concrete outcomes that can reflect the underlying, ongoing ethical input and validate the suitability of such a concept in a public-private partnership project will only be available in the second part of the project.

## 5. Conclusions

The PARADIGM “applied ethics” concept of early and ongoing engagement of EEP members in the WPs’ and Tasks’ from brainstorming to production process has been developed and implemented. The Ethics Framework has now been established.

## 6. Annexes

Declaration of Interests Form.



## PARADIGM Declaration of Interests: Disclosure Statement Year 2018-2019

Conflicts of interest may arise when an individual's personal, business, occupational or professional interests or loyalties conflict with the interests of the PARADIGM project, when writing or reviewing content or taking editorial decisions, and/or PARADIGM's principles on transparency, objectivity and independence. A conflict of interest occurs when, in the course of their PARADIGM activities, contributors are privy to PARADIGM decisions or documents that provide opportunities to obtain personal, business, economic, occupational or professional benefits for themselves and/or third parties.

Even though the project does not address any specific indication or treatment, PARADIGM is a public-private partnership project involving patients, pharmaceutical industry, academia, not-for-profit organisations and SMEs. Therefore, this project is based on utmost transparency. Public declaration and management of potential conflicts of interest are of major importance.

All members of the PARADIGM Steering Committee, Project Team, and Ethics Expert Panel, the Task Leaders and the main contacts for all members of the Consortium have to complete a personal interest disclosure form describing his/her professional and non-professional activities and affiliations. This form takes into consideration Section 3 of the [ICMJE's requirements for Disclosure of Potential Conflicts of Interest](#). It is subject to an update after 18 months or, on a voluntary basis, in case of new professional or non-professional activities.

The completed forms are made available to all PARADIGM participants and are provided upon request to external stakeholders. They are regularly reviewed by the Ethics Expert Panel. Identified potential conflicts of interest are reported to the PARADIGM Steering Committee for resolution.

Last name: \_\_\_\_\_

First name: \_\_\_\_\_

Postal address: \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

Tick as appropriate:

Member of

- **PARADIGM Consortium**
  - **PARADIGM Steering Committee, Project Team, EEP or Task Leader**
- Enter the name of the PARADIGM Committee(s)

\_\_\_\_\_  
 \_\_\_\_\_

I have read and understood the PARADIGM Ethics Framework.

I hereby state that I do not have any conflict of interest, financial or otherwise that may be seen as competing with the interests of PARADIGM or its principles on transparency, objectivity and independence.

If you are not sure whether one of your engagements might be of competing or conflicting interest with the interests of PARADIGM, please contact the Chair of the Ethics Expert Panel (contact details below) with an explanation of the situation. The EEP will decide on whether this disclosed interest creates any conflict for your active participation in PARADIGM.

### **Affirmation of Compliance**

I have received and carefully read the PARADIGM project's objectives and PARADIGM's Ethics Framework and have considered not only the literal expression of the policy, but also its intent. By signing this affirmation of compliance, I hereby affirm that I understand and agree to comply with the policy.

If any situation should arise in the future that I think may involve me in a conflict of interest, I will promptly and fully disclose in writing the circumstances to the PARADIGM Ethics Expert Panel.

I further certify that the information set forth in this Disclosure Statement is true and correct to the best of my knowledge, information and belief.

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

Please send a copy of your completed, signed and dated Disclosure Statement to the Chair of the Ethics Expert Panel:

EFGCP  
Attn: Ingrid Klingmann, MD, PhD  
Rue de l'industrie, 4  
1000 Brussels  
Belgium

Or as pdf to  
[Ingrid.klingmann@efgcp.eu](mailto:Ingrid.klingmann@efgcp.eu)